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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/529,967	04/24/00	KORPELA	M 2328-117

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EXAMINER	
SISSON, B	
ART UNIT	**PAPER NUMBER**
1655	11

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/529,967	Applicant(s) KORPELA ET AL.	
	Examiner Bradley L Sisson	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 June 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) *11-15 and 20-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 16-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Acknowledgment is made of applicant having amended non-elected claims, presented additional claims, as well as presented argument for rejoinder in their response of 25 June 2001. Rather than present claims that may have unity of invention at the time of responding to the election requirement, or at least prior to mailing of the first action on the merits, applicant chose to not to act in resolving any unity of invention issues via an amendment to the claims prior to receiving a first action on the merits.

2. Newly submitted claims 21 and 22, and by extension the amendment to claims 11 and 14, are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The method of claim 1 does not require the vector or host cell of claims 11 and 14.

3. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-15 and 20-22 have withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. This application contains claims 11-14 and 20-22 drawn to an invention nonelected with traverse in Paper No. 7. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Drawings

5. The figures remain objected to for reasons of record.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 and 16-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of *E. coli* K-12/pTetLux1 and *E. coli* K-12/TetLuc1 to detect the presence of tetracycline in the presence of culture broth as well as in spiked limpec porcine serum, does not reasonably provide enablement for the detection of any and all levels of tetracycline in any type of sample, regardless of its heterogeneity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *In re Wands*, 8 USPQ2d 1400 (CAFC 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Quantity of Experimentation Necessary

The quantity of experimentation need is great, on the order of several man-years and then with little, if any, reasonable expectation of success.

The Amount of Direction or Guidance Provided and The Presence or Absence of Working Examples

The amount of guidance provided is severely limited. As seen in Example 2, page 17 of the specification, a comparison was conducted between *E. coli* K-12/pTetLux1 and *E. coli* K-12/TetLuc1. In Example 3, (page 18, first paragraph) "fresh *E. coli* K-12/pTetLux1 were diluted 1:50 with 25 mM MES buffer in M9 minimal medium, pH 6.0. 100 µl bacterial suspension was added to microtiter plate wells containing 100 µl of pig serum spiked with different tetracyclines." Example 4 (page 18, second paragraph), like that of Example 3, teaches the use of *E. coli* K-12/pTetLux1 in detecting the presence of tetracyclines in milk to which has been added EDTA. The specification does not teach how one of skill should proceed in the testing of samples such as "fish, meat, infant formula, eggs, honey, vegetables, serum, plasma, whole blood or the like" (claim 10). The situation at hand is analogous to that in *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001. As set forth in the decision of the Court:

> " '[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation.' *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *see also Amgen Inc. v. Chugai Pharms. Co.*, 927 F. 2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed Cir. 1991); *In re Fisher*, 427 F. 2d 833, 166 USPQ 18, 24 (CCPA 1970) ('[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art.').
>
> *****

> "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (starting, in context of the utility requirement, that 'a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.') Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention.
> "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research. (emphasis added)

While the specification has been found to provide limited guidance, such guidance does not extend to the full scope for which patent protection is being sought. Accordingly, it would require undue experimentation for one of skill in the art to practice the full scope of the claims. Applicant is urged to consider narrowing the scope of the claims to those embodiments adequately supported by the disclosure.

The Nature of the Invention

The claimed invention relates directly to matters of physiology and chemistry, which are inherently unpredictable and as such, require greater levels of enablement. As noted in *In re Fisher* 166 USPQ 18 (CCPA, 1970):

> In cases involving predictable factors, such as that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.

The State of the Prior Art

The state of the art is limited in the area of recombinant mechanisms for the detection of tetracyclines.

The Relative Skill of Those in the Art

The relative skill of those in the art that is most closely associated with the claimed invention is high, on par with those that hold a Ph.D. in biochemistry.

The Breadth of Scope of the Claims

The claims have sufficient breadth of scope so to encompass any number of constructs that can be used in the detection of any level of tetracycline. As presently worded, the claimed method places no limitation on (a) the type of media used for culturing the transformant; (b) the type of transformant used; (c) the heterogeneity of the sample; (d) what means are used to determine just which tetracycline is present; (e) what means, if any, are employed so to determine the quantity of each tetracycline present; and (f) the level of sensitivity of the assay. In view of the breadth of scope of the claims now before the Office, the unpredictableness of the assay system, and the limited guidance provided, the level of effort needed to be exerted by the public in order to practice the full scope of the claimed method constitutes undue

experimentation. Accordingly, applicant is again urged to consider adopting claims that more closely align the scope of the claims with the level of disclosure provided.

Response to argument

At page 7 of the response received 25 June 2001, hereinafter the response, attorney for applicant provides a listing of references that are asserted as being demonstrative of the state of the art and thereby lowering the threshold for the quantity of experimentation needed. This argument has been fully considered and has not been found persuasive toward the withdrawal of the rejection as none of the articles have been considered on the merits as they have not been provided nor cited in an Information Disclosure Statement. Further, even if the documents had been provided, they do not take the place of sworn statements as to be found in a declaration.

Even if the above cited documents had been cited in the specification and had been incorporated by reference, the aspect of enablement would still not have been met as none of the documents are US patents and the disclosures contained within these documents may well be essential to the treatment and handling of specific starting materials, e.g., eggs, honey, vegetables, plasma, and whole blood. The specification provides five examples:

Example 1, page 16, reconstitution of freeze-dried *E. coli* K-12/pTetLux1;

Example 2, page 17, construction of different sensors;

Example 3, page 18, measurement of tetracycline levels in pig serum;

Example 4, page 18, measurement of tetracycline in milk using the chelator EDTA; and

Example 5, page 18, provides a description of Figure 11 as it relates to "the kinetics of bacterial bioluminescence after exposure of *E. coli* K-12/pTetLux1 to different dilutions of tetracycline antibiotics."

At best Examples 3 and 4 address the aspect of using pig serum and milk as a starting material. Upon closer inspection, however, not even these two examples are found to provide the reactions conditions used for each of the assays. Accordingly, one of skill in the art would be forced to develop and identify reproducible conditions whereby such methods can be practiced. To force the public into enabling the practice of a method is an improper shift of the burden of enablement away from that of applicant to the public as it is the application, not the public, that is to fully enable each and every claim. *Genentech v. Novo Nordisk A/S* 42 USPQ2d 1001.

Agreement is reached where at page 8, last paragraph, of the response it is asserted that the specification provides literal support for the use of other prokaryotic cells. However, the mere listing of potential alternative cells does not constitute an enabling disclosure for the use of same. At best, a listing of alternative materials can be an invitation for others to develop the assay such that these alternative embodiments can actually be used in a reproducible manner.

At page 10, last paragraph, of the response agreement is seemingly reached as to the level of skill in the art at the time the invention was made. However, the Office does not find persuasive that one of skill in the art should be forced to research and develop just how the claimed assay is to be practiced. As stated in *Genentech*:

> While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. "It is true . . . that a specification need not disclose what is well known in the art. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986). However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting

> that all the disclosure related to the process is within the skill of the art. It is the specification, not the knowledge of one skill in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement. This specification provides only a starting point, a direction for further research.

7. Agreement is seemingly also reached in that the claims do encompass a large number of alternative embodiments. However, rather than being able to point to how and where the specification enables the claimed invention, applicant's attorney of record again redirects one's attention to publications that are not of record. Any and all publications cited in the response and not provided in an Information Disclosure statement, have not been considered on the merits.

8. For the above reasons, and in the absence of convincing evidence to the contrary, the rejection is maintained.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bradley L Sisson whose telephone number is (703) 308-3978. The examiner can normally be reached on 6:30 a.m. to 5 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stephanie Zitomer can be reached on (703) 308-3985. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

B. L. Sisson

Bradley L Sisson
Primary Examiner
Art Unit 1655

bls
August 27, 2001